PROGRAM #:
1110 - B0530

CHARACTERIZATION OF THE DYNAMICS OF LIQUID AND GEL SPREAD IN THE SUPRACHOROIDAL SPACE OF ENUCLEATED PORCINE EYES

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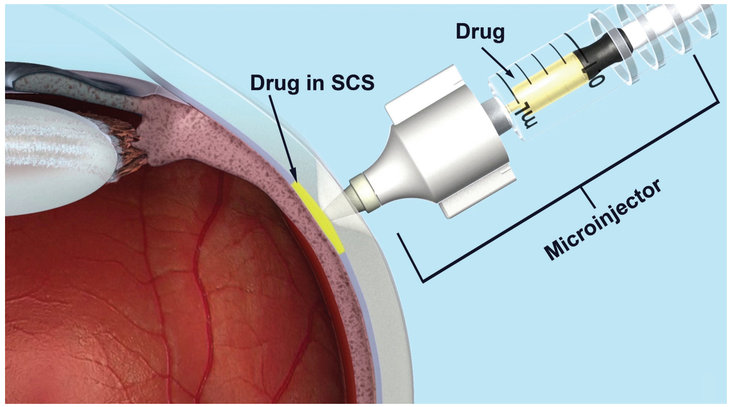
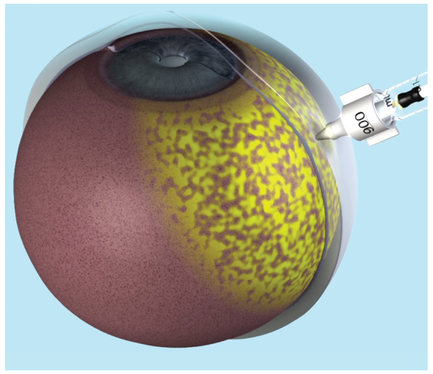
PURPOSE

To characterize the liquid and gel spread following suprachoroidal injections in enucleated porcine eyes.

INTRODUCTION

- Clearside Biomedical, Inc., headquartered in Alpharetta, GA, is a clinical-stage biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye.
- By choosing the appropriate drug or drug combination, potential treatments are being developed using suprachoroidal injection.
- Suprachoroidal dosing for the treatment of eye diseases has several potential advantages including high bioavailability, and differentiating efficacy and safety.
- Clearside currently has 4 development programs: a non-infectious uveitis program currently enrolling a Phase 3 clinical study; an RVO program currently enrolling a Phase 3 clinical study; a DME program that is currently enrolling a Phase 1/2 trial; and a pre-clinical neovascular AMD program.





Injected drug formulation spreads around the eye in the suprachoroidal space (SCS).

METHODS

Enucleated porcine eyes were acclimated to room temperature (~22 °C) with intraocular pressure (IOP) stabilized to 17±2 mmHg prior to injections. One percent Seakem LE agarose solution (solidifying @ <37 °C) was heated to ~100 °C and injected suprachoroidally at volumes ranging from 5 µL to 200 µL. Eye samples were dissected and analyzed two (2) minutes post-injection. Dimethyl sulfoxide (DMSO) was injected suprachoroidally at room temperature (~22 °C) with volumes ranging from 1 µL to 10 µL. Eye samples in this test group were immediately frozen to -36 °C for approximately 5 minutes and dissected post-injection for analysis. Ultraviolet (UV) fluorescent particles were added to each formulation batch prior to injections to enhance visualization of spread. Image analysis was performed to characterize and quantify spread of formulations in a gel state.

RESULTS

Area of gel coverage ranged from 0.1 cm^2 to 2.1 cm^2 in agarose injections, volumes ranging from 5 µL to 200 µL. Injections <50 µL resulted in roughly symmetrical spread profiles, but displayed more circumferential spread as injection volume increased to ≥50 µL. Average gel thickness calculations ranged between 0.4 mm to 1 mm with the assumption of uniform gel thickness. Gel coverage for DMSO was observed to occupy a larger area compared to that seen from agarose with 0.1 cm^2 to 0.8 cm^2 ranges in spread for 1 µL to 10 µL injection volumes.

FIGURE 1. DMSO SPREAD FROM A 1 µL SUPRACHOROIDAL INJECTION

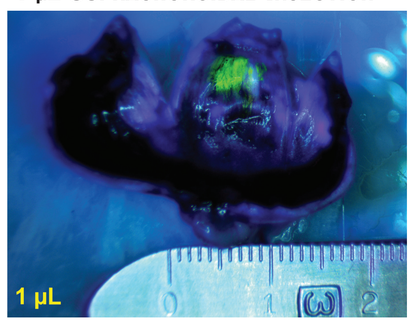


FIGURE 2. DMSO SPREAD FROM A 10 µL SUPRACHOROIDAL INJECTION

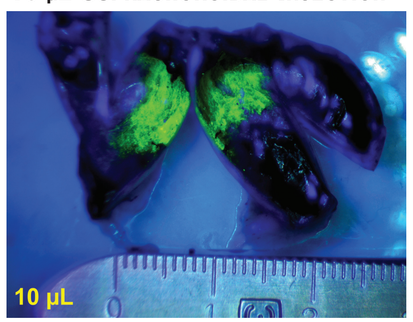


FIGURE 3. DMSO SPREAD FROM A 50 µL SUPRACHOROIDAL INJECTION

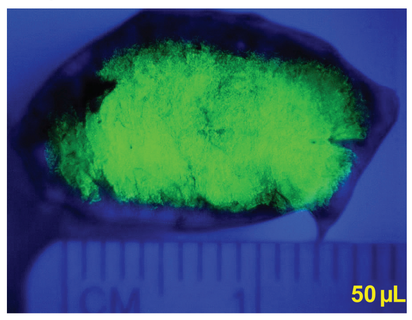
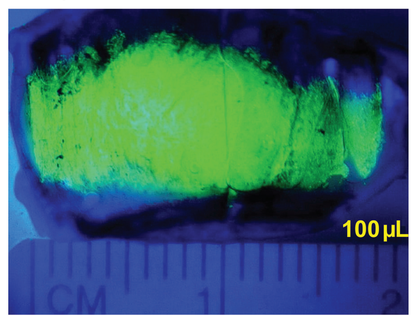
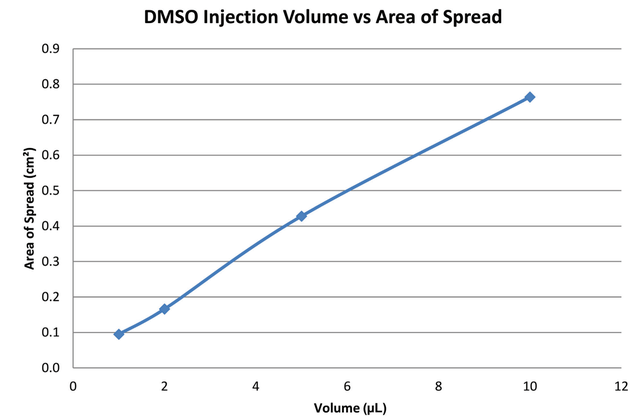


FIGURE 4. DMSO SPREAD FROM A 100 µL SUPRACHOROIDAL INJECTION

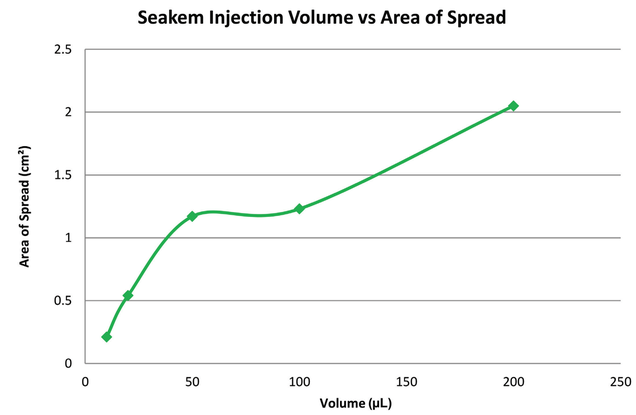


RESULTS

GRAPH 1. SUPRACHOROIDAL SPREAD OF SEAKEM INJECTION



GRAPH 2. SUPRACHOROIDAL SPREAD OF DMSO INJECTION



CONCLUSIONS

- Spread profiles of formulations delivered suprachoroidally were captured within seconds after injection.
- Suprachoroidal injections with Seakem LE agarose displayed more circumferential spreading at injection volumes greater than 50 µL which may be due to the anatomical landscape of the Suprachoroidal Space.
- Higher spread coverage seen in DMSO may be attributable to a relative lower viscosity.
- This study shows that suprachoroidally injected fluids rapidly cover a relatively large area, as much as a few squared centimeters, within a few seconds of administration.
- Less viscous formulations may cover a greater area of spread compared to more viscous formulations when delivered suprachoroidally.

Website: www.clearsidebio.com